

### REMARKS

Favorable reconsideration of the subject application, as amended, is respected requested in view of the comments below.

Claims 1-16 are pending in the present application. Claims 1 and 6 have been replaced with new claims 17 and 18. Accordingly, claims 2-5, 7-16, 17 and 18 are presented for examination on the merits.

The specification has been amended to correct a minor typographical error.

Claims 1 and 6 have been rewritten in order to more particularly define the claimed invention. In particular, new claim 17 clarifies the position of the various amino acid substitutions and insertions that may be made in prenyl diphosphate synthase to provide the mutants of the present invention. According to claim 17 the mutant prenyl diphosphate synthase synthesizes prenyl diphosphate which is shorter than prenyl diphosphate synthesized by a corresponding wild-type enzyme. This latter amendment is fully supported by the disclosure at page 10, lines 33-36.

Claim 6 has been rewritten as new claim 18 to more particularly define the properties that are retained by the claimed mutants. Support for new claim 18 is found at page 12, lines 9-20, where it is disclosed that the enzymatic activities and thermostability of prenyl diphosphate synthase is retained in the present mutants.

Accordingly, no new matter is added by the amendments to the claims.

It is respectfully submitted that the amendments to claims 1 and 6 above render the rejection of claims 1-16 and rejection of claim 6 under 35 U.S.C. §112, second paragraph moot.



Claims 1-16 are rejected under 35 U.S.C. §102(a) as being anticipated by Ohnuma, et al (N).

Applicants enclose herewith a verified translation of Japanese Application No. 8-213211, filed July 24, 1996, from which the present application claims priority under 35 U.S.C. §119. Accordingly, the rejection of claims 1-16 under 35 U.S.C. §102(a) is rendered moot.

Claims 1-16 are rejected under 35 U.S.C. §102(b) as being anticipated by Ohnuma et al. (AZ). The Examiner states that the present claims encompass mutants having an amino acid substitution at the fifth amino acid upstream of the first aspartic acid residue of the aspartic acid-rich domain I (amino acid position 77), which corresponds to amino acid 81 of *Bacillus stearothermophilus* geranylgeranyl diphosphate synthase. Ohnuma et al. disclose an amino acid substitution at position 81. The Examiner concludes, therefore, that the cited reference anticipates the present claims.

Applicants respectfully disagree with the Examiner's conclusion.

Ohnuma (AZ) discloses a mutant *Bacillus stearothermophilus* farnesyl diphosphate synthase. Native farnesyl diphosphate synthase synthesizes farnesyl diphosphate, whereas Ohnuma's mutant enzyme synthesizes geranylgeranyl diphosphate, which is longer than farnesyl diphosphate. (See Figure 3 of the cited reference). Thus, the mutation in Ohnuma's farnesyl diphosphate synthase results in an enzyme that synthesizes a longer product than the wild-type enzyme.

In contrast, the mutation in the presently claimed farnesyl diphosphate synthase results in a product, farnesyl diphosphate, which is shorter than wild-type farnesyl diphosphate. As disclosed at page 10, lines 33-36, the claimed mutant "can synthesize a farnesyl diphosphate having a shorter chain length than the prenyl

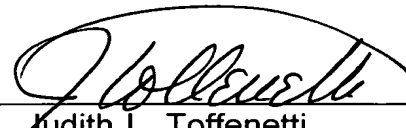
diphosphate synthesized by the native prenyl diphosphate synthase." (Page 10, lines 33-36). The synthesis of a shorter product was demonstrated in Example 5. In Example 5, the activity and reaction product of wild-type and the claimed mutant prenyl diphosphate synthase were compared. As can be seen in Figure 3, native enzyme, SacGGPS, produces geranylgeranyl diphosphate (GGOH), whereas the claimed mutants, including those having a mutation at amino acid 77, produce a significantly shorter product, farnesyl diphosphate (FOH). Thus, the present mutant enzymes do not produce the same product as Ohnuma's mutant and therefore, are not anticipated by the cited reference.

Accordingly, it is respectfully submitted that the present application, as amended, is in condition for allowance, an early notification thereof being earnestly solicited.

The Commissioner is authorized to charge any fees relevant to this filing, under 37 CFR §§1.16 and 1.17, to Kenyon & Kenyon Deposit Account 11-0600.

Respectfully submitted,

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Judith L. Toffenetti  
Reg. No. 39,048

KENYON & KENYON  
1025 Connecticut Avenue, NW  
Washington, DC 20036  
telephone: 202/429-1776  
facsimile: 202/429-0796

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